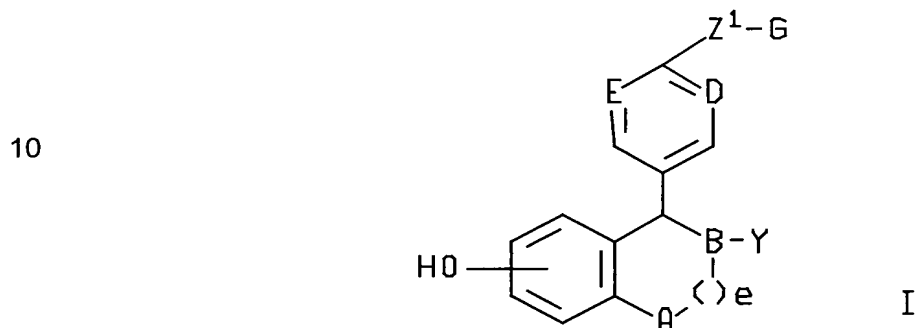


# CLAIMS

What is claimed is:

1. A method of preventing breast cancer in a mammal which comprises  
5 administering to a mammal in need of such prevention an effective amount of a compound of the formula I:



15 wherein:

A is selected from CH<sub>2</sub> and NR;

B, D and E are independently selected from CH and N;

Y is

- 20 (a) phenyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (c) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;
- 25 (d) C<sub>3</sub>-C<sub>8</sub> cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- 30 (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>; or

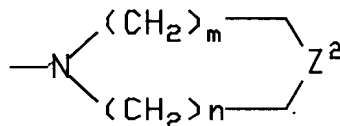
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>-, NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

Z<sup>1</sup> is

- (a) -(CH<sub>2</sub>)<sub>p</sub> W(CH<sub>2</sub>)<sub>q</sub>-;  
 (b) -O(CH<sub>2</sub>)<sub>p</sub> CR<sup>5</sup>R<sup>6</sup>-;  
 (c) -O(CH<sub>2</sub>)<sub>p</sub>W(CH<sub>2</sub>)<sub>q</sub>-;  
 (d) -OCHR<sup>2</sup>CHR<sup>3</sup>-; or  
 (e) -SCHR<sup>2</sup>CHR<sup>3</sup>-;

G is

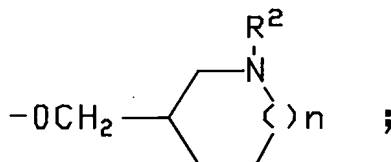
- (a) -NR<sup>7</sup>R<sup>8</sup>;  
 (b)



wherein n is 0, 1 or 2; m is 1, 2 or 3; Z<sup>2</sup> is -NH-, -O-, -S-, or -CH<sub>2</sub>-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R<sup>4</sup>; or

- (c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

Z<sup>1</sup> and G in combination may be



W is

5

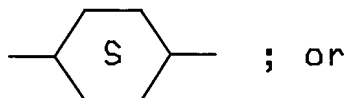
- (a)  $-\text{CH}_2-$ ;
- (b)  $-\text{CH}=\text{CH}-$ ;
- (c)  $-\text{O}-$ ;
- (d)  $-\text{NR}^2-$ ;
- (e)  $-\text{S}(\text{O})_n-$ ;
- (f)

10



- (g)  $-\text{CR}^2(\text{OH})-$ ;
- (h)  $-\text{CONR}^2-$ ;
- (i)  $-\text{NR}^2\text{CO}-$ ;
- (j)

15



- (k)  $-\text{C}\equiv\text{C}-$ ;

R is hydrogen or  $\text{C}_1\text{-C}_6$  alkyl;

20

$\text{R}^2$  and  $\text{R}^3$  are independently

- (a) hydrogen; or
- (b)  $\text{C}_1\text{-C}_4$  alkyl;

$\text{R}^4$  is

25

- (a) hydrogen;
- (b) halogen;
- (c)  $\text{C}_1\text{-C}_6$  alkyl;
- (d)  $\text{C}_1\text{-C}_4$  alkoxy;
- (e)  $\text{C}_1\text{-C}_4$  acyloxy;
- (f)  $\text{C}_1\text{-C}_4$  alkylthio;
- (g)  $\text{C}_1\text{-C}_4$  alkylsulfinyl;
- (h)  $\text{C}_1\text{-C}_4$  alkylsulfonyl;
- (i) hydroxy ( $\text{C}_1\text{-C}_4$ )alkyl;
- (j) aryl ( $\text{C}_1\text{-C}_4$ )alkyl;
- (k)  $-\text{CO}_2\text{H}$ ;

30

- (l) -CN;  
 (m) -CONHOR;  
 (n) -SO<sub>2</sub>NHR;  
 (o) -NH<sub>2</sub>;  
 5 (p) C<sub>1</sub>-C<sub>4</sub> alkylamino;  
 (q) C<sub>1</sub>-C<sub>4</sub> dialkylamino;  
 (r) -NHSO<sub>2</sub>R;  
 (s) -NO<sub>2</sub>;  
 (t) -aryl; or  
 10 (u) -OH.

R<sup>5</sup> and R<sup>6</sup> are independently C<sub>1</sub>-C<sub>8</sub> alkyl or together form a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring;

R<sup>7</sup> and R<sup>8</sup> are independently

- (a) phenyl;  
 15 (b) a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring, saturated or unsaturated;  
 (c) a C<sub>3</sub>-C<sub>10</sub> heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;  
 (d) H;  
 (e) C<sub>1</sub>-C<sub>6</sub> alkyl; or  
 20 (f) form a 3 to 8 membered nitrogen containing ring with R<sup>5</sup> or R<sup>6</sup>;

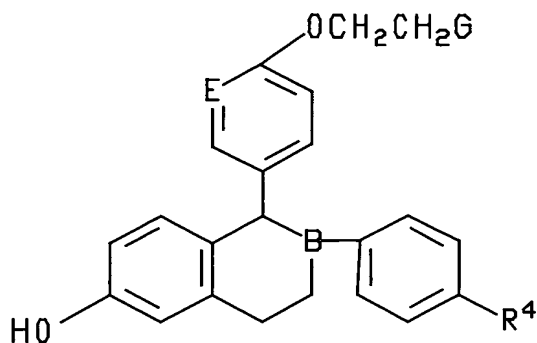
R<sup>7</sup> and R<sup>8</sup> in either linear or ring form may optionally be substituted with up to three substituents independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, alkoxy, hydroxy and carboxy;

- a ring formed by R<sup>7</sup> and R<sup>8</sup> may be optionally fused to a phenyl ring;  
 25 e is 0, 1 or 2;  
 m is 1, 2 or 3;  
 n is 0, 1 or 2;  
 p is 0, 1, 2 or 3;  
 q is 0, 1, 2 or 3;

30 and optical and geometric isomers thereof; and nontoxic pharmacologically acceptable acid addition salts, N-oxides, esters, and quaternary ammonium salts thereof.

2. A method of claim 1 wherein the compound is a compound of the formula:

5



3. A method of preventing breast cancer in a mammal which comprises administering to a mammal in need of such prevention an effective amount of (-)-*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol, or a nontoxic pharmacologically acceptable acid addition salt, N-oxide, ester, or quaternary ammonium salt thereof.
- 10 4. A method of preventing breast cancer in a mammal which comprises administering to a mammal in need of such prevention an effective amount of *Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol, or an optical or geometric isomer thereof; or a nontoxic pharmacologically acceptable acid addition salt, N-oxide, ester, or quaternary ammonium salt thereof.
- 15